



Clinical trial results:

Evaluation of the use of an oral direct anti-Xa anticoagulant, Apixaban in prevention of venous thromboembolic disease in patients treated with IMiDs during myeloma: a pilot study

Summary

EudraCT number	2013-003190-99
Trial protocol	FR
Global end of trial date	08 August 2016

Results information

Result version number	v1 (current)
This version publication date	18 June 2022
First version publication date	18 June 2022

Trial information

Trial identification

Sponsor protocol code	38RC13.410
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02066454
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CHU de GRENOBLE
Sponsor organisation address	CS 2017, GRENOBLE, France,
Public contact	Directrice générale du CHU de GRENOBLE, CHU de Grenoble, 33 0476768455, ARCPromoteur@chu-grenoble.fr
Scientific contact	Directeur général du CHU de GRENOBLE, CHU de Grenoble, 33 0476768455, ARCPromoteur@chu-grenoble.fr

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 June 2017
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	08 August 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate:

- the incidence of venous thromboembolic event (VTE)
- the incidence of hemorrhagic complications,

In a population of patients with myeloma who are treated with IMiDs and require thromboprophylaxis for 6 months, using an oral anti-Xa anticoagulant, Apixaban, in a preventive scheme, 2.5 mg x2/day

Protection of trial subjects:

An independent oversight committee will be established.

It will be led by 4 people: 2 vascular doctors, 1 hematologist and 1 pharmacovigilant.

Its role is to:

- Monitor the frequency of events (critical events and ISGs).
- Give an opinion on the continuation or not of the trial (premature termination, continuation of inclusions, request for an interim analysis) based on the data provided by the biostatistician of the CIC of Grenoble

This committee will meet in the following cases:

- occurrence of 5 events validated by the validation committee of the type thromboembolic event, arterial event, hemorrhage or death
- occurrence of an unexpected serious adverse reaction or SUSAR
- occurrence of an adverse reaction with an unusual frequency
- all 50 patients included

It may also be convened at the initiative of the promoter and the event validation committee. It shall keep the sponsor and the Scientific Committee informed of its conclusions in writing.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 January 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 108
Worldwide total number of subjects	108
EEA total number of subjects	108

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	107
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

105 patients, from the centres of the Intergroupe Francophone du Myélome (IFM),

Pre-assignment

Screening details:

After determining the type of myeloma treatment and deciding to initiate thromboprophylaxis, the inclusion and non-inclusion criteria of the study having been verified, the biological and ultrasound data of the screening collected, patients are then eligible for the study treatment, Apixaban

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

non applicable

Arms

Arm title	one arm
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Arm description:

Apixaban, 2.5 mgx2 / day, for 6 months

Arm type	1 arm
Investigational medicinal product name	Apixaban
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Buccal tablet
Routes of administration	Buccal use

Dosage and administration details:

Apixaban, 2.5 mgx2 / day, for 6 months

Number of subjects in period 1	one arm
Started	108
Completed	84
Not completed	24
non included	4
Premature discontinuation	20

Baseline characteristics

Reporting groups

Reporting group title	overall trial
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Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	108	108	
Age categorical			
Units: Subjects			
Adults (18-64 years)	40	40	
From 65-84 years	68	68	
Gender categorical			
Units: Subjects			
Female	52	52	
Male	56	56	

End points

End points reporting groups

Reporting group title	one arm
Reporting group description: Apixaban, 2.5 mgx2 / day, for 6 months	

Subject analysis set title	One Arm
Subject analysis set type	Full analysis
Subject analysis set description: evaluate the incidence of venous thromboembolic event and the incidence of hemorrhagic complications	

Primary: evaluate the incidence of venous thromboembolic event and the incidence of hemorrhagic complications

End point title	evaluate the incidence of venous thromboembolic event and the incidence of hemorrhagic complications
End point description: Total venous thromboembolism (fatal or nonfatal PE, symptomatic distal or proximal DVT of lower limbs, asymptomatic proximal DVT detected by bilateral compression ultrasound and VTE-related death) and major or clinically relevant nonmajor bleeding	
End point type	Primary
End point timeframe: All patients received apixaban, 2.5 mg x 2/day for 6 months, and were monitored monthly for 7 months (clinical parameters—pulse, blood pressure, biochemistry—blood count, renal function, hepatic parameters).	

End point values	one arm	One Arm		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	104	104		
Units: yes				
number (confidence interval 95%)	0.38 (0.05 to 1.4)	0.38 (0.05 to 1.4)		

Statistical analyses

Statistical analysis title	Primary endpoint
Comparison groups	one arm v One Arm
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0
Method	incidence of VTE
Parameter estimate	clinical outcomes during treatment

Adverse events

Adverse events information

Timeframe for reporting adverse events:

At each visit until end of study

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21
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Reporting groups

Reporting group title	intervention
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Reporting group description:

Apixaban, 2.5 mgx2 / day, for 6 months

Serious adverse events	intervention		
Total subjects affected by serious adverse events			
subjects affected / exposed	29 / 104 (27.88%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Plasmacytoma			
subjects affected / exposed	6 / 104 (5.77%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fracture			
subjects affected / exposed	2 / 104 (1.92%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	6 / 104 (5.77%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Diplopia			

subjects affected / exposed	2 / 104 (1.92%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Lung disorder			
subjects affected / exposed	2 / 104 (1.92%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Pain			
subjects affected / exposed	7 / 104 (6.73%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	5 / 104 (4.81%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	intervention		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	52 / 104 (50.00%)		
Infections and infestations			
Infection			
subjects affected / exposed	52 / 104 (50.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 March 2014	Addition of 1 center: Daniel HOLLARD Institute and 1 investigator
20 March 2014	Addition of a center: Centre Hospitalier d'Avignon Principal Investigator :D r SLAMA Borhane
14 October 2014	Change of principal investigator of the Centre Hospitalier La Côte Basque: Principal Investigator: Dr RANDRIAMALALA Edouard
15 October 2014	Addition of 2 centers: RENNES and AMIENS Update: - the diagram of the study, - the Ecog inclusion criterion >2, - precision on the 1st EchoDopler made between D-7 and J-1 - the date of the meeting of the Supervisory Committee, - contact details of vigilance/Promoter, - the definition of the events seen by the event validation committee d
03 December 2014	Addition of a centre and a principal investigator for the Beausoleil Clinic centre Associate Investigator: Dr Sophie AUGER QUITTET
12 January 2015	Addition of a centre and a principal investigator for the Blois hospital centre Associate Investigator: Dr Abderrazak EL YAMANI
09 June 2015	Addition of 4 centers: Lucien Neuwirth Cancer Institute// Principal Investigator :D r Augeul-Meunier Chartres Hospitals// Principal Investigator: Dr MAIGRE Hôpital sévigné Cesson RENNES// Principal investigator: Dr BAREAU CH MACON// Principal Investigator: Dr RAICHON
20 July 2015	Addition of 2 centers: University Cancer Institute TOULOUSE// Principal Investigator :P r ATTAL CHU ESTAING CLERMONT FERRAND// Principal Investigator: DR CHALETEIX

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported